



Complete Summary

GUIDELINE TITLE

(1) Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (2) 2007 addendum. (3) 2009 addendum.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (amended). London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Aug 01. 84 p. (Technology appraisal guidance; no. 111).

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously published: National Institute for Health and Clinical Excellence (NICE). Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (amended). London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Sep. 62 p. (Technology appraisal guidance; no. 111).

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SCOPE

DISEASE/CONDITION(S)

Alzheimer's disease (AD)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Geriatrics
Internal Medicine
Neurology
Pharmacology
Psychiatry

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To provide an update review of the best quality evidence for the clinical effectiveness and cost-effectiveness of donepezil, rivastigmine, and galantamine for mild to moderately-severe Alzheimer's disease (AD)
- To provide a review of the best quality evidence for the clinical effectiveness and cost-effectiveness of memantine for moderately-severe to severe AD

TARGET POPULATION

Patients with Alzheimer's disease (AD)

Note: Patients with other forms of dementia (for example, vascular dementia or dementia with Lewy bodies) are not included.

INTERVENTIONS AND PRACTICES CONSIDERED

1. Acetylcholinesterase inhibitors
 - Donepezil
 - Galantamine
 - Rivastigmine
2. Memantine (recommended only as part of well designed clinical trials)

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
 - Global functioning
 - Cognition
 - Function
 - Behaviour and mood
 - Health-related quality of life
 - Ability to remain independent

- Likelihood of admission to residential/nursing care
- Carer health related quality of life
- Compliance (adherence)
- Adverse events
- Cost effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
 Hand-searches of Published Literature (Secondary Sources)
 Searches of Electronic Databases
 Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Southampton Health Technology Assessment Centre (SHTAC), University of Southampton. (See the "Availability of Companion Documents" field.)

Clinical Effectiveness

Data Sources

Electronic databases were searched from inception to July 2004. Bibliographies of included studies and related papers were checked for relevant studies and experts were contacted for advice and peer review and to identify additional published and unpublished studies. Manufacturer submissions to the National Institute for Health and Clinical Excellence were reviewed.

Study Selection

Studies were included if they met the following criteria.

- Interventions: donepezil, rivastigmine, galantamine, or memantine.
- Participants: people diagnosed with Alzheimer's disease who met the criteria for treatment with donepezil, rivastigmine, galantamine, or memantine.
- Design: systematic reviews of randomised controlled trials (RCTs) and RCTs comparing the different drugs with placebo or each other or non-drug comparators were included in the review of effectiveness. Economic evaluations including a comparator (or placebo) and both the costs and consequences (outcomes) of treatment were included.
- Primary outcomes: measures of global functioning, cognition, function, behaviour and mood, and health related quality of life.

Studies in non-English language were excluded. Studies published only as abstracts or conference presentations were included if sufficient detail was presented. Titles and abstracts were screened for eligibility by one reviewer and checked by a second reviewer. Inclusion criteria were applied to the full text of selected papers by two reviewers. Any differences in opinion were resolved through discussion or consultation with a third reviewer.

Cost Effectiveness

Methods for the Systematic Review of Economic Evaluations

A systematic literature search was undertaken to identify economic evaluations comparing donepezil, rivastigmine, galantamine, and memantine plus best supportive care, with best supportive care alone (or with one another). The details of databases searched and search strategy are documented in Appendix 3 of the Assessment Report (see the "Availability of Companion Documents" field). Manufacturers' and Sponsors' submissions to NICE were reviewed for additional studies.

Titles and abstracts of studies identified by the search strategy were assessed for potential eligibility by two reviewers, with any disagreement resolved through discussion and referral to a third reviewer if necessary. The full text of relevant papers was obtained and inclusion criteria applied.

Economic evaluations were eligible for inclusion if they reported on the cost-effectiveness of included pharmaceuticals patients with Alzheimer's Disease (AD), in the licensed indication.

In some instances studies that did not meet the inclusion criteria for the review of clinical effectiveness are included in the review of cost-effectiveness.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

- **Donepezil:** Thirteen published randomized controlled trials (RCTs) and one unpublished RCT were included.
- **Rivastigmine:** Four published and two unpublished RCTs were included.
- **Galantamine:** Six published RCTs and one unpublished RCT were included.
- **Memantine:** Two published RCTs were included.

Cost Effectiveness

- **Donepezil:** Nine published economic evaluations of donepezil and the industry submission were included, together with two published abstracts.
- **Rivastigmine:** Four published economic evaluations of rivastigmine and the industry submission were included, plus one published abstract.
- **Galantamine:** Five published economic evaluations of galantamine (industry sponsored) plus the industry submission were included.
- **Memantine:** Two published (in-press) economic evaluations and the industry submission were included, plus three published abstracts.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Southampton Health Technology Assessment Centre (SHTAC), University of Southampton. (See the "Companion Documents" field.)

Data Extraction and Quality Assessment

Data extraction and quality assessment were undertaken by one reviewer and checked by a second reviewer, with any differences in opinion resolved through discussion. The quality of included randomized controlled trials (RCTs) was assessed using criteria developed by the National Health Service (NHS) Centre for Reviews and Dissemination. An outline assessment of economic evaluations was undertaken using a standard checklist.

Data Synthesis

The clinical and cost-effectiveness data were synthesised through a narrative review with full tabulation of the results of included studies. Where appropriate meta-analysis of data was undertaken.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Twenty-one published economic evaluations of the three acetylcholinesterase (AChE) inhibitors and memantine were available to the Appraisal Committee. All four manufacturers also submitted their own economic evaluations. The Assessment Group reran each of the manufacturer's economic models using its preferred assumptions, and it also presented an additional economic evaluation of the three AChE inhibitors. Further analyses were undertaken by the National Institute for Health and Clinical Excellence (NICE) secretariat as described in technical report number 1 and the addendum of the Assessment Report (see the "Availability of Companion Documents" field).

See section 4.2 in the original guideline document for more details about the cost analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the National Institute for Health and Clinical Excellence (NICE): On August 26, 2009, NICE announced that, following consultation with stakeholders on the economic model that underpinned NICE's 2006 guidance on the use of drugs to treat Alzheimer's disease, the resulting guidance remains unchanged.

In accordance with the Court of Appeal's ruling on the economic model used in the technology appraisal of drugs for the treatment of Alzheimer's disease, NICE released the fully executable version of the model to stakeholders for their comment in November 2008. Having fully reviewed all the resulting comments the independent Appraisal Committee concluded that, although a number of technical inaccuracies were highlighted and amendments were made to the economic model, these were not sufficient to change the original conclusion that these treatments are not cost effective in the mild stages of the disease. Consultees then had a chance to appeal against this decision but no appeals were received.

NICE guidance on the use of donepezil, galantamine, rivastigmine, and memantine for the treatment of Alzheimer's disease therefore remains unchanged and the drugs continue to be recommended only for people with moderate Alzheimer's disease.

Guidance

This guidance applies to donepezil, galantamine, rivastigmine, and memantine within the marketing authorisations held for each drug at the time of this appraisal; that is:

- Donepezil, galantamine, rivastigmine for mild to moderately severe Alzheimer's disease
- Memantine for moderately severe to severe Alzheimer's disease

The benefits of these drugs for patients with other forms of dementia (for example, vascular dementia or dementia with Lewy bodies) have not been assessed in this guidance.

1.1 The three acetylcholinesterase inhibitors donepezil, galantamine, and rivastigmine are recommended as options in the management of patients with Alzheimer's disease of moderate severity only (that is, subject to section 1.2 below, those with a Mini Mental State Examination [MMSE] score of between 10 and 20 points), and under the following conditions:

- Only specialists in the care of people with dementia (that is, psychiatrists including those specialising in learning disability, neurologists, and physicians specialising in the care of the elderly) should initiate treatment. Carers' views on the patient's condition at baseline should be sought.
- Patients who continue on the drug should be reviewed every 6 months by MMSE score and global, functional, and behavioural assessment. Carers' views on the patient's condition at follow-up should be sought. The drug should only be continued while the patient's MMSE score remains at or above 10 points (subject to Section 1.2 below) and their global, functional, and behavioural condition remains at a level where the drug is considered to be having a worthwhile effect. Any review involving MMSE assessment should be undertaken by an appropriate specialist team, unless there are locally agreed protocols for shared care.

When using the MMSE to diagnose moderate Alzheimer's disease, clinicians should be mindful of the need to secure equality of access to treatment for patients from different ethnic groups (in particular those from different cultural backgrounds) and patients with disabilities.

1.2 In determining whether a patient has Alzheimer's disease of moderate severity for the purposes of section 1.1 above, healthcare professionals should not rely, or rely solely, upon the patient's MMSE score in circumstances where it would be inappropriate to do so. These are:

- Where the MMSE is not, or is not by itself, a clinically appropriate tool for assessing the severity of that patient's dementia because of the patient's

learning or other disabilities (for example, sensory impairments) or linguistic or other communication difficulties

Or

- Where it is not possible to apply the MMSE in a language in which the patient is sufficiently fluent for it to be an appropriate tool for assessing the severity of dementia, or there are similarly exceptional reasons why use of the MMSE, or use of the MMSE by itself, would be an inappropriate tool for assessing the severity of dementia in that individual patient's case.

In such cases healthcare professionals should determine whether the patient has Alzheimer's disease of moderate severity by making use of another appropriate method of assessment. For the avoidance of any doubt, the acetylcholinesterase inhibitors are recommended as options in the management of people assessed on this basis as having Alzheimer's disease of moderate severity.

The same approach should apply in determining for the purposes of section 1.1 above, and in the context of a decision whether to continue the use of the drug, whether the severity of the patient's dementia has increased to a level which in the general population of Alzheimer's disease patients would be marked by an MMSE score below 10 points.

1.3 When the decision has been made to prescribe an acetylcholinesterase inhibitor, it is recommended that therapy should be initiated with a drug with the lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started). However, an alternative acetylcholinesterase inhibitor could be prescribed where it is considered appropriate having regard to adverse event profile, expectations around concordance, medical comorbidity, possibility of drug interactions, and dosing profiles.

1.4 Memantine is not recommended as a treatment option for patients with moderately severe to severe Alzheimer's disease except as part of well designed clinical studies.

1.5 Patients with mild Alzheimer's disease who are currently receiving donepezil, galantamine, or rivastigmine, and patients with moderately severe to severe Alzheimer's disease currently receiving memantine, whether as routine therapy or as part of a clinical trial, may be continued on therapy (including after the conclusion of a clinical trial) until they, their carers, and/or specialist consider it appropriate to stop.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on randomized, controlled trials, systematic review, and published economic evaluations.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of donepezil, galantamine, rivastigmine and memantine for the treatment of patients with Alzheimer's disease
- Potential benefits may be demonstrated on measures of global functioning, cognition, function, behaviour and mood, and health related quality of life. These drugs may also improve the ability to remain independent, reduce the likelihood of admission to residential/nursing care, and improve carer health related quality of life.

POTENTIAL HARMS

- Typical side effects of donepezil, galantamine, and rivastigmine are related to the gastrointestinal tract (including nausea and vomiting). These side effects are dose related and although they are usually short term they can lead to non-adherence.
- In clinical trials in mild to severe dementia, involving patients treated with memantine and patients treated with placebo, the most frequently occurring adverse events with a higher incidence in the memantine group than in the placebo group were dizziness, headache, constipation and somnolence. These adverse events were usually of mild to moderate in severity.

For full details of side effects, precautions, and contraindications, see the Summary of Product Characteristics, available at <http://emc.medicines.org.uk/>.

CONTRAINDICATIONS

CONTRAINDICATIONS

For full details of side effects, precautions, and contraindications, see the Summary of Product Characteristics, available at <http://emc.medicines.org.uk/>.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organizations in meeting core and developmental standards set by the Department of Health in "Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by the National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "Healthcare Standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on the NICE website (<http://guidance.nice.org.uk/TA111> [see also the "Availability of Companion Documents" field]).
 - Costing report and costing template to estimate the savings and costs associated with implementation
 - Audit criteria to monitor local practice (see appendix C of the original guideline document).

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources
Slide Presentation

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (amended). London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Aug 01. 84 p. (Technology appraisal guidance; no. 111).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Jan (revised 2006 Nov; addenda released 2007 Sep and 2009 Aug)

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor Andrew Stevens (*Chair*), Professor of Public Health, University of Birmingham; Professor David Barnett (*Vice Chair*) Professor of Clinical Pharmacology, University of Leicester; Dr Jane Adam, Department of Diagnostic Radiology, St George's Hospital; Professor A E Ades, MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol; Dr Tom Aslan, General Practitioner, Stockwell, London;Â Mrs Elizabeth Brain, Lay Member; Dr Karl Claxton, Professor of Health Economics, University of York; Mrs Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool; Dr Paul Ewings, Statistician, Taunton & Somerset NHS Trust, Taunton;Â Professor John Geddes,

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously published: National Institute for Health and Clinical Excellence (NICE). Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (amended). London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Sep. 62 p. (Technology appraisal guidance; no. 111).

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (amended). Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Sep. 4 p. (Technology appraisal 111). Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease. Costing report and template. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Sep. Various p. (Technology appraisal 111). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Dementia. Slide set. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Sep. 39 p. (Technology appraisal 111). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (amended). Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Aug. 10 p. (Technology appraisal 111). Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- The clinical and cost-effectiveness of donepezil, rivastigmine, galantamine, and memantine for Alzheimer's disease. Assessment Report. Southampton Health Technology Assessment Centre (SHTAC); 2005 Mar. Electronic copies: Available from the [NICE Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1142. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Donepezil, galantamine, rivastigmine and memantine for Alzheimer's disease. Understanding NICE guidance (amended). Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Sep. 6 p. (Technology appraisal 111).

Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](http://www.nice.org.uk).

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1143. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on February 16, 2007. It was updated in response to the September 2007 addendum on October 5, 2007, and again in response to the August 2009 addendum on December 4, 2009.

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